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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/780,532	02/09/2001	Clive Wood	GNN-012CP	8383

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02/27/2006

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EXAMINER

QIAN, CELINE X

ART UNIT PAPER NUMBER

1636

DATE MAILED: 02/27/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/780,532	Applicant(s) WOOD ET AL.	
	Examiner Celine X. Qian Ph.D.	Art Unit 1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 01 December 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 2,3,5-8,39-43 and 45-65 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 2,3,5-8,39-43 and 45-65 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 05 July 2001 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Claims 2, 3, 5-8, 39-43, 45-65 are pending in the application.

This Office Action is in response to the Amendment filed on 12/1/05.

Response to Amendment

The rejection of claim 40 under 35 U.S.C. 112 2nd paragraph has been withdrawn in light of Applicant's amendment.

The rejection of claims 2, 3, 5-8, 39-43, 45-65 under 35 U.S.C. 112 1st paragraph is maintained for reasons set forth of the record mailed on 6/1/05 and further discussed below.

Response to Arguments

In response to the written description rejection, Applicants argue that the amended claims are directed to methods of modulating NFkB activity by contacting cell with TRADE polypeptides containing the extracellular domain of a TRADEa polypeptide and having the ability to modulate activity of the TRADEa polypeptide. Applicants assert that the specification discloses more than one species of TRADE polypeptides having the claimed features, thus the description of the invention is adequate.

This argument has been fully considered but deemed unpersuasive. The specification defines TRADE polypeptide as a TNF Receptor family member Associated with Death domain protein, which has a TRADE structural domain (see page 9, lines 10-25). However, the TRADE structural domain is not defined in the specification. As such, this family potentially encompasses a large number of polypeptides may not even have TRADEa function. The claims are directed to a TRADE polypeptide comprises the extracellular domain of a TRADEa polypeptide that has 95% sequence identity with 1-168 of SEQ ID NO:2. Applicants are

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reminded that the claimed genus is a polypeptide agent comprises the extracellular domain of a TRADEa having 95% sequence identity with 1-168 of SEQ ID NO:2, which encompasses a large number of polypeptides of various length and property/function as long as they comprising a domain share 95% sequence similarity with 1-168 of SEQ ID NO:2. As discussed in the previous office action, the cytosolic domain which is C-terminal of SEQ ID NO:2 is responsible for stimulation of NFkB activity. The specification fails to describe a polypeptide that comprises 1-168 of SEQ ID NO:2 or 95% similar to SEQ ID NO:2 having NFkB stimulatory function. As such, the specification fails to describe the claimed genus by a representative number of species by their complete structural and other identifying characteristics.

With regard to Applicants' argument that several species of the claimed genus have been described, Applicants are reminded that not only all of them are arguments of SEQ ID NO:2, but also longer than the claimed domain 1-168. Furthermore, according to the disclosure of the specification and Figure 14, the TRADE 198 and TRADE 218 hardly have any stimulatory effect on NFkB. Moreover, the disclosed species is hardly representative of the entire claimed genus which includes a large number of polypeptides of various length and property/function as long as they comprising a domain share 95% sequence similarity with 1-168 of SEQ ID NO:2. As such, for reasons discussed in the previous office action and above, the specification fails to provide sufficient written description to the claimed invention. Therefore, this rejection is maintained.

In response to the enablement rejection, Applicants argue that the specification provides multiple examples of polypeptides having modulation features. Applicants assert that all these polypeptides comprises TRADEa extracellular domain are able to modulate NFkB promoter driven luciferase activity, thus they clearly fall within the limitation of the present claims.

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Applicants further argue that since all these polypeptides that modulates the NFkB construct comprises the extracellular domain of the TRADEa, thus it is not unpredictable if they can modulate NFkB signaling. Applicants further assert that the specification clearly establishes a nexus between the claimed method and the modulation of NFkB, and the modulation of TRADEa because Applicants successfully modulated NFkB transcription using various TRADEa polypeptides. Applicants further assert that one skill in the art would also understand that the claimed invention would be useful for treating and preventing any disease that would benefit from the modulation of TRADEa activity or NFkB signaling. Applicants further assert the method is also useful for identifying agents that modulate TRADEa activity or expression. Applicants thus conclude that the instant claims are enabled.

Applicants' argument are fully considered but deemed unpersuasive. The detailed reasons of the non-enablement of the claimed method were discussed in the previous office action. As discussed above, the specification defines TRADE polypeptide as a TNF Receptor family member Associated with Death domain protein, which has a TRADE structural domain (see page 9, lines 10-25). However, the TRADE structural domain is not defined in the specification. As such, this family potentially encompasses a large number of polypeptides, wherein their function of modulating NFkB signaling is unpredictable based on the teaching of the specification. With regard to Applicants' argument of multiple example of polypeptide, Applicants are reminded that not only all of them are fragments of SEQ ID NO:2, but also longer than the claimed domain 1-168. Such disclosure is not sufficient to support the broad claim scope of a polypeptide comprises 95% sequence similarity to 1-168 of SEQ ID NO:2, which encompasses a large number of polypeptides of various length and property/function as long as

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they comprising a domain share 95% sequence similarity with 1-168 of SEQ ID NO:2. Contrary to Applicants' assertion, although there is a nexus between the TRADEa consists sequence of SEQ ID NO:2, the specification fails to establish that a polypeptide comprises 95% sequence similarity to 1-168 of SEQ ID NO:2 also have such nexus. Furthermore, the specification fails to disclose that a polypeptide comprises 95% sequence similarity to 1-168 of SEQ ID NO:2 have modulating effect toward any TRADEa molecule. Lastly, with regard to Applicants' argument of using the claimed method to modulate TRADEa expression/activity *in vitro*, Applicants are again reminded that the specification does not establish such modulatory function of any polypeptide comprises 95% sequence similarity to 1-168 of SEQ ID NO:2 toward the TRADEa molecule expression and activity. Since prior art is silent on the teaching of the TRADE and its modulatory function and the specification does not teach such self-regulatory function of the TRADEa molecule, one skilled in the art would have to engage in undue experimentation to practice the method as claimed. Therefore, this rejection is maintained.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period

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will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celine X. Qian Ph.D. whose telephone number is 571-272-0777. The examiner can normally be reached on 9:30-6:00 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel Ph.D. can be reached on 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Celine X Qian Ph.D.
Examiner
Art Unit 1636

**CELIAN QIAN
PATENT EXAMINER**

